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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,248	03/07/2000	Sergio Abgrignani	CHIR-0234	9892

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	22

DATE MAILED: 06/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/520,248	Applicant(s) ABGRIGNANI, SERGIO
	Examiner Ron Schwadron, Ph.D.	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08/776,259* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/28/2001 has been entered.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3 Claims 5 and 6 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. applicants arguments have been considered and deemed not persuasive.

Claims 5 and 6 are indefinite in that it is unclear to what the recited dosages refer. It is unclear whether said dosage refers to a dosage of 100U/ml of IL-2 wherein the concentration refers to concentration of IL-2 in the dose administered to a subject, or whether it refers to the concentration of IL-2 in the blood or tissue fluid following administration and distribution into these compartments or what said dosage means.

Regarding applicants comments, the specification, page 10, lines 11-25 refers to an in vitro experiment. It provides no explanation as to what the dosage recited in the claims means in the context of in vivo administration. There is no disclosure in the specification as to what the dosage recited in the claims means in the context of an in vivo method and said dosage has no art recognized meaning in the context of an in vivo method.

4. Regarding the term "contacting the T cell independent of antigen" as recited in the claims, said phrase is interpreted as meaning that the cytokines are administered without also administering antigen. It does not mean that the host is free of antigen at the time of administration because this is physically impossible. An antigen would

encompass any bacterial or viral antigen. All humans contain a variety of normally occurring bacterial/viral antigens such as bacterial proteins found in the gut produced by bacteria which reside in the gut of all humans (see Guarner et al). Similarly, the vast majority of humans are infected with EBV or CMV, wherein said viruses produce various viral proteins (see Kapoor et al). An antigen would also encompass allergens (pollen, etc.) to which all humans are exposed.

Furthermore, regarding the term "antigen independent activation of T cells", the art recognizes that the antigenic specificity of T cells is predetermined by the TCR and that T cells with the entire permitable predetermined spectrum of specificities are present in any normal individual. The administration of the cytokines recited in the claims would therefore inherently activate T cells for which no antigen was present because no individual will contain every antigen for which a responsive T cell is present.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 3-6 and 10-12 stand rejected under 35 U.S.C. 102(b) as being anticipated by Chong, (U.S. Patent 4,879,111). Applicants arguments have been considered and deemed not persuasive.

Chong discloses a method of administration of IL-2 and TNF-alpha for treatment of infections (see abstract). Chong discloses that the IL-2 and TNF-alpha can be administered before the presence of bacterial antigen (see abstract). Therefore, said administration is independent of antigen. Although the dosages recited in the claims are unclear for the reasons discussed above in the rejection under 112/2 the dosages

given in column 5 of the Chong appear to be comparable to the dosages recited in claims 5 and 6 based on functional activity . The method inherently results in antigen independent activation of T cells because the method has the same steps as the claimed method. The cells recited in claims 3 and 4 are present in vivo in humans (as are all possible types of immune cells which would be present in any individual in the absence of a specific genetic defect that would result in the absence of a particular cell population).

Regarding applicants comments, Chong discloses that the administration of IL-2 and TNF-alpha can be before bacterial antigen (see abstract). Therefore, said administration is independent of antigen. Applicants comments involve various limitations not currently recited in the claims. Chong discloses a method of administration of IL-2 and TNF-alpha for treatment of infections (see abstract). Chong discloses that the administration of IL-2 and TNF-alpha can be before bacterial antigen (see abstract). Therefore, said administration is independent of antigen. The claims currently do not recite any limitation that is not disclosed in Chong. Regarding applicants comments about the dosage, in view of the fact that said dosage is not even defined in the specification or has any meaning in view of the prior art, it is unclear as how applicant can say that said dosage differs from the prior art.

7. Claims 1, 3-6 and 10-12 stand rejected under 35 U.S.C. 102(e) as being anticipated by Zimmerman et al. (U.S. Patent 5,425,940). Applicants arguments have been considered and deemed not persuasive. Zimmerman et al. disclose administration of a combination of IL-2 and TNF-alpha for treatment of tumors, see abstract. The dosages describe in col. 6 of the cited patent appear to fall within the same ranges as the dosages of IL-2 and TNF-alpha recited in instant claims 5 and 6, based on functional activity . The combination of IL-2 and TNF-alpha are administered independent of antigen (they are administered without administration of antigen). The method inherently results in antigen independent activation of T cells because the method has the same steps as the claimed method. The cells recited in claims 3 and 4 are present in vivo in humans (as are all possible types of immune cells which would be present in any individual in the absence of a specific genetic defect that would result in the absence of a particular cell population).

Regarding applicants comments, the combination of IL-2 and TNF-alpha are administered independent of antigen (they are administered without administration of antigen). Applicants comments are also addressed in paragraphs 6 and 4 of this Office Action.

8. No claim is allowed.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644